INSTITUTE: National Institute of Environmental Health Services

STUDY NUMBER: 94-E-0165 PRINCIPAL INVESTIGATOR: Lisa G. Rider, M.D.

STUDY TITLE: Studies in the Natural History and Pathogenesis of Childhood-Onset and Adult-Onset Idiopathic Inflammatory Myopathies

Continuing Review Approved by the IRB on 09/28/10
Amendment Approved by the IRB on 09/28/10 (S) Date Posted to Web: 11/03/10
Adult Patient

INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

You have been referred to the National Institutes of Health for evaluation of myositis, a condition involving inflammation in the muscles. Because of the inflammation, damage to muscle and other organs may occur, resulting in significant disability. The cause of myositis is not yet known, but it is believed to involve an alteration in the immune system leading to the inflammation.

You are being asked to give permission to participate in a study designed to advance our knowledge about myositis and related conditions. We are inviting children and adults with myositis and related conditions to participate in a study to understand better what causes the disease and what alterations occur in the immune system, to define better the specific problems which occur in patients with myositis, and to learn what signs, symptoms and tests can predict how a patient will respond to therapy. You will **not** receive treatment for your medical conditions at NIH at this time or in the future when you become ill. The physicians involved in this study do **not** plan to provide treatment or to take over your medical care. Taking part in the study is entirely voluntary and personal benefit to you may not result from your

participation, but knowledge may be gained that will benefit others. You are free to withdraw your consent and to discontinue your participation in this study at any time without prejudice.

All clinical information about your illness obtained from participation in the study will become part of your medical record. This thorough clinical evaluation of the extent and severity of your condition may help us and your doctor in planning the best treatment for your illness. Blood samples (serum, plasma, and white blood cells), urine and biopsy materials may be used for laboratory research studies, and will be stored for future research. Tissue samples that have been surgically removed previously and are no longer needed for clinical care will be collected for the study protocol. This includes muscle and skin biopsies, calcinosis samples, and biopsies of other internal organs, as well as available tissue blocks. Your blood and urine samples with their name on them will be processed in the NIH and by our contractors for testing and for storage in a freezer. We will store all your samples with a code and not with your name. Coding is done to protect your identity and only those researchers closely involved with the progress of the study will have access to the locked files that can link the code to your name or other private information. Protocol investigators may also receive coded clinical information obtained as part of the research study to link to a blood, urine or tissue sample. Coded samples on occasion may be supplied to investigators outside of NIH for additional research. These samples will always be coded with a number so that you will not be identifiable to outside investigators.

Some blood samples will be used for isolating and studying DNA (genetic material), and some DNA will be stored for future study. We will compare the DNA from people with myositis to the DNA from people without those diseases to find the differences that exist. We plan to study many parts of the DNA, which together make up what is called the genome. By newly available techniques, called genome wide association studies, we expect to identify many of the genetic changes associated with myositis. Since we also will combine genetic information with information from medical records, such as features of the illness or different people's responses to treatments, this project could lead to more knowledge about myositis and why certain people develop certain complications or respond differently to a treatment. With such knowledge, future treatments may be developed. Treatments may even be individualized to reflect a patient's unique genetic make-up. The results of your genome-wide DNA studies will be placed in a government health research database available on the internet, combined with information from all of the other subjects enrolled in this study. Specific genetic data from you as an individual would be available only to qualified approved researchers and these researchers would not have access to traditional identifying information about you. Further information about this DNA database and the associated risks are discussed below on pages 9-10. It is possible that the researchers will learn new information that may link the changes seen in your blood samples to a specific condition or disease and this could affect your ability to obtain health and life insurance or a job in the future. NIH and the Clinical Center, like other hospitals, may be required to release such information to insurance companies if you have signed a release of information form. We will provide any clinically-relevant results of all studies to your referring physician. The investigators conducting this study do not plan to provide your physician with the results of any medical tests or evaluations or other information pertaining to your illness which are not clinically relevant, because the results will be preliminary and will require further analysis; further research may be necessary before these results are meaningful. The results of genetic testing will generally not be available to you or placed in your medical record, because the clinical relevance and importance of these results will generally not be clear. If meaningful information is developed from this study that may be important for your health, you will be recontacted when it becomes available to see if you want to learn more. By agreeing to participate in this study, you do not waive any rights that you may have regarding access to and disclosure of your records. For further information on those rights, please contact Dr. Rider.

Study Procedure and Your Involvement

An adult with myositis or related conditions may participate in one or two parts of the study. You may participate in the medical record review, history physical examination outlined in (1). Alternatively, you may come to participate in this, as well as a thorough 3 to 7 day clinical evaluation, outlined in (2) below. In each case, you may choose to be evaluated one time at NIH or may return for one or two follow-up evaluations over a one year period.

1. Medical Record Review, History, Physical Examination

For this portion of the study, you will fill out a standard release of medical information form from the NIH and send it to your doctors. This will allow your doctors to make your medical records available to us, including allowing us to review any previous biopsy materials and radiography obtained from you. This also authorizes us to contact your physician if we have specific medical questions about your past medical history. A referring physician for you must be identified prior to your participation in this study, and your past medical records must be received by the principal investigator prior to your visit to NIH.

You will undergo a one-day evaluation in the outpatient clinic at the National Institutes of Health. The evaluation will consist of taking a medical history, including completing some questionnaires, performing a physical examination. This evaluation is performed to document the features and status of your myositis, the responses to treatments, and to explore factors that may have contributed to illness onset or flare. We will also collect a sample of urine and blood for routine clinical and special research tests (up to 12 tablespoons or 150 ml blood for research). The amount of blood drawn will conform to NIH limits, which are 10.5 ml per kg or 550 ml (1.25 pints), whichever is smaller, every 8 weeks for adults; this is considered to be a safe amount. The hazards of blood drawing primarily involve the pain of the needle puncturing the skin and the risk of getting a bruise. Depending upon your condition, and to assist us in accurately diagnosing your illness or planning the best treatment, other procedures may be suggested for you.

The blood testing you will undergo includes tests of muscle enzymes and other blood and urine chemistries; autoantibodies that may be seen in patients with myositis and other autoimmune diseases; tests of blood vessel function; genes for human leukocyte antigens (HLA) and cytokine polymorphisms and other genes that may relate to the development of myositis or to certain complications that some patients develop; blood and urine markers to see if any are associated with active myositis or can tell myositis apart from other autoimmune diseases; and research tests to see if there are cells from your mother are circulating in your blood. If you receives prednisone or a related medication, a blood level of prednisone may be tested one hour after the morning dose, along with blood tests related to its metabolism. By studying each subject's entire genome, new genetic risk factors for myositis may be identified. Additional studies of specific genes may be undertaken in the future to understand more about their role in the development of myositis. Some blood and urine will be stored for additional research studies not described here. Some of these tests, not all, will be repeated at follow-up evaluations.

As part of this evaluation, you may have a test on your urine to check for pregnancy. . If this test is positive, you will be notified of the results and you will not be eligible to participate in the clinical evaluation of this study outlined below. This is because pregnancy will complicate the interpretation of immune activation markers, which is part of the assessment of disease activity. We would, however, make sure you received appropriate counseling and will be referred for medical treatment for this.

For patients participating in this study through their local health care provider, if you agree to participate in this study, you will be enrolled during a visit to your local health care provider. This evaluation will involve obtaining your medical records for our review, answering questions about your medical history, completing written questionnaires, undergoing a physical examination and having your physician complete a questionnaire about your illness, and donating blood, urine and possibly other clinical specimens, including muscle biopsy, calcinosis samples and other tissues, for research purposes. All this information and your blood and urine samples, as well as tissue samples, will be returned to the NIH or its designees for processing using a kit which we have sent to your local health care provider. When we receive this kit, you and your local health care provider will each receive $100 to compensate you for your time and expenses. In order to process your samples at the NIH, you will first complete and sign a form, which gives us your contact information and permission to do these studies and assigns you an NIH number.

2. Clinical Evaluation

In addition to undergoing a history, physical examination, and blood and urine tests as outlined above, you may choose to come to the National Institutes of Health for additional clinical evaluation of your condition. This evaluation would last 3 to 7 days; follow-up evaluation may occur 1 or 2 times in a one year period. Whenever your health permits, this evaluation would be done as an outpatient, although you will need to be admitted to a ward in the hospital if you require an EMG study or muscle biopsy. This clinical evaluation, which would assess the extent and severity of your illness, is detailed below. The main aspects of this clinical evaluation, including assessments of muscle strength, physical function, muscle enzymes, and other aspects of your myositis or longstanding changes related to the illness, will be stored in a database that will be accessible with permission to myositis researchers. The purpose of this database is to pool outcome measure, response to treatment and basic information about patient's illnesses from a number of clinical trials and natural history studies, in order to develop better outcome measures for myositis, to learn more about their illnesses, and to perform pooled analyses of treatment responses.

Standardized Muscle Strength Testing: A physiotherapist in the Department of Rehabilitation Medicine would perform standardized muscle strength testing in order to see how strong you are; these tests may be repeated by the physician evaluating you. The physiotherapist or physiatrist will also do an analysis of your walking (gait), including the amount of distance you can walk in a 6 minute period of time, and examine the range of motion of your joints. You will also be asked to fill out several questionnaires about your ability to perform daily tasks and your overall well being. Additional muscle strength testing will be performed to more accurately measure muscle strength, in which the limb is moved at maximal force against a machine with weights. A muscle power test will also be obtained to see how much work your muscles can perform by moving a weight as rapidly as possible against variable resistance. You will be asked general questions about your overall energy level. With the muscle power test, there is a small risk of experiencing muscle soreness within 48 hours of the test. If you have underlying heart disease or high blood pressure, you will be excluded from the muscle power test.

Electrocardiogram: This is a test measuring the electrical activity of your heart. Wires are attached to the chest wall, arms and legs using a sticky paste which takes only a few seconds. There is no discomfort from this procedure. If the electrocardiogram shows any abnormalities, an echocardiogram, or sound-wave study of your heart function would also be done. No harmful consequences of this procedure are known.

Pulmonary Function Tests: Your lung function and breathing would be assessed by this test if you are having any difficulties with breathing. You would have to blow into a tube for a few seconds, but some cooperation is needed. If this test shows abnormalities, a chest x-ray or chest CT scan would also be obtained.

Swallowing and Speech Studies: You will be asked to fill out a questionnaire to see if the myositis has affected your speech or ability to swallow and handle secretions. If you are experiencing any problems with voice or swallowing, t he Department of Rehabilitation Medicine would also perform studies of your tongue strength and endurance and examine the mouth and swallowing tube using non-invasive techniques. You would also have an ultrasound swallowing study; no harmful effects of ultrasound are known. If these studies are abnormal or you have had alot of stomach and intestinal pain or bleeding, a barium swallow study would also be done.

For patients in whom the speech-language pathologist has observed changes in voice quality or resonance (such as hoarseness, harshness, nasality), you will be offered the possibility to undergo a more thorough voice evaluation to assess the vocal cords and surrounding muscles. This extensive voice evaluation will include a computerized voice analysis using tape recordings of your voice and indirect laryngoscopy by an otolaryngologist. This last procedure involves a small rigid scope placed in the mouth to look directly at the vocal cords; a small videocamera would also record how the vocal cords are functioning. The potential benefits of these procedures are to understand the full extent of the voice/vocal cord abnormalities and to aid in planning treatment and voice therapy. During the laryngoscopy exam, some

patients may experience a strong tendency to gag, which can be treated by using an anesthetic which is sprayed in the nose or mouth. If you experience severe discomfort, the procedure will be stopped.

Skin Evaluation: A thorough evaluation of how the myositis is affecting your skin will be made by the physicians seeing you; whenever possible, a dermatologist will also see you. If the dermatologist finds that you have some skin rashes which may require more intensive medical treatment of the myositis, photographs of the lesions may be taken and a skin biopsy would be done on these lesions in order to confirm their pathology. Photographs of the nail fold capillaries may also be taken using a droplet of oil for magnification. Photographs of skin rashes, nail fold capillaries and other findings are taken for a number of purposes, including for research, to teach other health care professionals and trainees about myositis, and for research publications and institute reports, including in medical journals and on the internet. The possibility exists that you may be identifiable in some of the photographs. For the skin biopsy, the skin is numbed with topical (EMLA cream) or an anesthetic injected under the skin (1% xylocaine with or without epinephrine). Following this, a sterile tiny blade is used to cut into the skin about 1/8 inch. This plug of skin is then cut free with a small scissors and placed in a test tube. Hazards of the numbing medicines include allergic reactions; other hazards are extremely unlikely unless there is absorption of the medicine into the bloodstream, and include an irregular heart rhythm and stimulation or depression. Hazards of the skin biopsy itself include the slight risks of infection or bleeding at the site, pain with the insertion of the needle, and the possibility of scarring at the site of biopsy and itching during healing. If there is a question whether you have recently developed calcium deposits under the skin (calcinosis) and if knowing this information would change the medicines that you receive, then you may undergo a CT scan to assess if calcinosis is present.

Brachial artery flow mediated dilation: If you have undergone certain blood tests to evaluate the blood vessels, then a test of the blood vessel function may also be performed. While lying down, an ultrasound machine will take a picture of your large blood vessel in the arm. A blood pressure cuff will then be tightened or inflated on your arm to try to make the blood vessel shrink in size. The blood pressure cuff will then be deflated, and then the rush of blood through the vessel will be examined by the ultrasound machine. After 15 minutes, you will receive a medicine called nitroglycerin by spraying a small amount under the tongue to try to further relax the blood vessels, and additional pictures will be taken with the ultrasound machine. During this test, you may experience some tingling or discomfort in the arm or leg, which resolves rapidly after the blood pressure cuff is deflated. Nitroglycerin can cause a few side effects, especially headache, and less commonly slowing of the heart rate, light-headedness, fainting, heartburn, a rash on the tongue, and low platelet count. You will be carefully monitored during and after this test.

Nutrition Assessment: A dietitian will measure how much body fat and muscle mass you have. This will be done by tape measurements or by bioelectrical impedance analysis. This involves attaching wires to the arms and legs using a sticky paste which takes only a few seconds. There is no discomfort from this procedure and no known harm. The purpose of this assessment is to measure muscle mass/muscle atrophy; this is not a nutrition/dietary consult.

Ophthalmologic Exam: If you are having symptoms of vision loss or other eye symptoms, or if you have evidence of extensive inflammation of the blood vessels (vasculitis) in other organs, an ophthalmologic exam may be performed to evaluate for vasculitis and inflammation in the retina.

Magnetic Resonance Imaging Scan and Spectroscopy of Lower Extremities: This research study produces a picture of your muscles or the tissue under the skin (subcutaneous tissue) using magnetism. The test involves having you lie on a padded table, which is slowly moved into a large tube inside the machine where there is a powerful magnet. Watches, keys, coins, bank and credit cards, certain types of jewelry cannot be brought into the room with the machine because of the power of the magnet. You will have to lie very still for the test, approximately 30-50 minutes. This test involves no x-rays and there are no known risks from the test, although some people may feel anxious about being in a small space (claustrophobic). If you are unable to lie still for at least 30 minutes for this test, you will not be able to undergo this

evaluation, but may participate in other aspects of the study. Some patients may undergo a second MRI test to look at all of the inflammation involved throughout their body (called whole-body MRI) and other patients may have a MRI test to look in more detail to see if the fat tissue under the skin is inflamed. Each of these tests would be up to 60- 90 minutes in duration.

Following conventional MRI of the lower extremities, MRI of muscle will be performed to assess muscle blood vessel density and blood flow in a second research test. A standard contrast agent called gadolinium will be injected by vein using a power injector. Scans will be obtained every 10 seconds for approximately 8 minutes following injection. The MRI contrast injection is associated with the pain of needle placement, and mild bruising can result when the needle is removed. Occasionally, headaches or nausea may result from these injections, and in very rare cases, serious reactions with shortness of breath or low blood pressure may occur. The US Food and Drug Administration has issued a warning that administration of gadolinium, the contrast imaging agent used in this protocol, has been associated with development of a disease called nephrogenic systemic fibrosis. The syndrome is rare (approximately 200 cases reported worldwide as of December, 2006 out of several million administrations of gadolinium), but disabling and in some cases, fatal. All cases to date have occurred in patients with severe kidney failure, including patients on dialysis. We will ask you whether you have or have had kidney disease or diabetes, whether you take diuretics (water pills) for any medical condition and whether you have received x-ray dye or drugs recently that might affect your kidney function. Depending on your history and measurement of a substance called creatinine in a blood sample, you may not be able to receive gadolinium.

Muscle Ultrasound: This study produces a picture of your thigh muscles using ultrasound or sound waves in order to examine the muscle structure, function and blood flow. You will have to lie very still for the test, which may take less than 60 minutes, and you will be asked to also tighten or contract their thigh muscles. The thigh will be measured while lying on your back, and a pen mark will be drawn on the leg muscle to mark the landmarks of the muscle. A small ultrasound transducer (a wand like tube) and a water gel, which may feel cold or wet, will be placed on the skin of the thigh and the transducer will be moved slowly along the marked line to obtain pictures. If you have no medical contraindications to exercise, you will be requested to repetitively climb a small step until you feel tired, or for a maximum of 10 minutes. Your heart rate and blood pressure will be monitored. Images will be obtained while you are lying still, when you contract your thigh muscle, and after stair stepping exercise. There are no known risks to this procedure.

Evaluation of Insulin Resistance, Lipodystrophy and other Endocrine Aspects: Insulin resistance, an abnormality in blood sugar processing, and less frequently, lipodystrophy, the loss and/or redistribution of body fat, are becoming recognized as conditions associated with juvenile dermatomyositis. Additional blood testing may be performed to evaluate the blood sugar and fat metabolism status in all myositis patients, when clinically indicated. This will include blood testing for glucose and insulin following a 12 hour fast, as well as lipids (total cholesterol, HDL, LDL, triglycerides, lipoprotein lipase), anti-insulin receptor antibodies and leptin; An endocrinologist will assess each patient when blood tests are abnormal. For patients with evidence of insulin resistance or body fat loss, a 2 hour oral glucose tolerance test will be performed to evaluate the insulin and sugar metabolism in more detail. In this test, you fast for 12 hours and then drink a sugar solution. Blood is taken at defined time points during the two hour period, usually through an intravenous catheter that is placed at the beginning of the test. Patients with evidence of body fat loss will also undergo additional testing as clinically indicated, which may include a liver ultrasound to assess for fatty infiltration or ovarian ultrasound to assess for cystic changes.

Other Procedures: When clinically indicated, additional testing may be recommended for you, including an electromyography study and a muscle biopsy. These procedures require separate informed consent and will be further explained to you if they are recommended.

Frequency of Testing: You may choose to have a one-time evaluation at NIH or return for repeat evaluations two or three times over a one-year period. You may choose to return for the limited exam or for the complete 3 to 7 day evaluation. At the return evaluation, physician examination, blood and urine tests, physical and occupational assessment of muscle strength, skin assessment, brachial artery flow mediated dilation, bioelectrical impedance analysis will be performed. Radiographic studies (chest x-ray, MRI of lower extremities, spectroscopy, swallowing studies), lung (pulmonary function tests), and heart studies (electrocardiogram, echocardiogram) and detailed voice evaluation (voice analysis, laryngoscopy) or endocrine evaluation (blood testing for insulin, lipids and other hormones; bone age; ultrasound of liver or ovaries) will be repeated only if the study at last evaluation was abnormal or as necessary for specific medical problems.

For all of these procedures, you will be consulted in advance, given full information, and asked to approve the specific plan. If you do not approve, the procedure will not be done.

You will **not** receive treatment for your myositis at NIH at this time or in the future when you become ill from the myositis. The physicians involved in your care at NIH will **not** take over your clinical care. We will, however, work with your referring physician and continue to make treatment recommendations to that doctor. You may potentially benefit directly from participation in this study by undergoing a very thorough clinical evaluation, the results of which will be shared with your doctor in order to help them plan the most appropriate treatments for you. The results of the DNA testing will not be of direct benefit to you, but will likely help researchers and health professionals around the world to better understand the causes of myositis, so that they can find better ways to prevent, detect, treat, and cure these illnesses.

We plan to re-contact you and/or your referring physician on one occasion after your visits to NIH to obtain follow-up information about additional treatment and responses to treatment, new clinical features, and outcomes.

WHAT WILL HAPPEN TO THE SAMPLES OR INFORMATION THAT ARE COLLECTED FROM THIS STUDY

Your DNA/blood/cell/urine/other samples/study records will remain stored indefinitely in order to allow for the studies to be completed and to allow for retesting of the samples as necessary. Your DNA/blood/cell/urine/and other samples will be stored at two sites: the National Institutes of Health and the repository of the National Institute of Environmental Health Sciences. The reason for duplication of long-term storage is to insure against accidental loss of frozen samples. All stored DNA/blood/cell/urine samples and information generated from this study will be identified by a code and not your name. This code will be kept secure in a locked area or in computer files that only Dr. Rider and a few specific investigators or their designees in this study can access with a password. Your coded samples or information may be sent to other investigators involved in this protocol for research purposes, as defined in this protocol. These investigators will not know your name and will not know which samples are yours. These collaborating investigators are located at: the National Institutes of Health, Bethesda, MD and Research Triangle Park, NC; the Center for Drugs Evaluation and Research, FDA in Bethesda and Silver Spring, MD; National Institute of Standards and Technology, Gaithersburg, MD; the Oklahoma Medical Research Foundation in Oklahoma City, OK; Oregon State University, Corvallis, OR; the Feinstein Institute for Medical Research in Manhasset, NY; MD Anderson Cancer Center in Houston, TX; the Baylor Institute for Immunology Research, Dallas TX; and the IWK Grace Health Science Center in Halifax, Canada; University of Manchester, Manchester and Salford, Engsland; Karolinska Institute, Stockholm, Sweden; Institute of Rheumatology, Prague, Czech Republic; University College, London, England and Children's Hospital Medical Center, Cincinnati, OH. Additional collaborating institutions may be involved in the future.

As part of this protocol, some of the data is stored coded in controlled access databases in which protocol investigators with approval have access to the data; your information is coded and you cannot be personally identified. In addition, a larger database is being created to pool outcome measures, responses to treatment and basic information about patients' illnesses from a number of clinical trials and natural history studies, in order to develop better outcome measures for

myositis, to learn more about these illnesses, and to perform pooled analyses of treatment responses. In this database, known as the International Myositis Assessment and Clinical Studies (IMACS) Group, all subjects' information will also be de-identified and coded. When data is transferred to investigators with approved projects, all subjects' information will be anonymized in this database and no identifying information about you will be provided to these investigators

Coded information from your DNA testing, known as genome-wide association studies, will be put in a government health research database, available on the Internet. Aggregate data that combines all participants in this study would be available to anyone on the internet. Your individual coded medical information and information from more detailed analyses of the coded samples will be put in a controlled-access database. The information in this database will be available in a secured manner only to qualified researchers who have received approval from an NIH Data Access Committee. *Please note that traditionally-used identifying information about you, such as your name, address, telephone number, or social security number, will NOT be put into the public genetic databases for this project and will also not be available to these approved researchers.*

Your samples will not be available for routine care or commercial diagnostic testing. It is possible that your samples or study records may be shared anonymously with other investigators for other research use beyond the scope of this study. Such usage will be strictly anonymous, in that no identifying information about you, including your name, will be provided to the researcher, and there will be no way for the researchers to link these samples back to you.

Your privacy is very important to us and we will use many safety measures to protect your privacy. However, in spite of all of the safety measures that we will use, we cannot guarantee that your identity will never become known. Under Federal law, anyone has a right to request the release of an individual's coded data (data that does not contain personally identifiable information) from the genome-wide database, including members of the public, insurers, employers and law enforcement agencies. NIH would take a legal position that this data is not releasable, but it is unclear that this would be upheld in court. Although your genetic information is unique to you, you share some genetic information with your children, brothers, sisters, and other blood relatives. Consequently, it may be possible that genetic information from them could be used to help identify you. Similarly, it may be possible that genetic information from you could be used to help identify them. While the public genetic databases developed for this project will **NOT** contain information that is traditionally used to identify you, such as your name, address, telephone number, or social security number, people may develop ways in the future that would allow someone to link your genetic information in these databases back to you. For example, someone could compare information in these genetic databases with information from you (or a blood relative) in another database and be able to identify you (or your blood relative).

Since some genetic variations can help to predict the future health problems of yourself and your relatives, this information might be of interest to employers, health providers, insurance companies, and others. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her blood relatives. Therefore, your genetic information potentially could be used in ways that could cause you or your family distress, such as by revealing that you (or a blood relative) carries a genetic disease or by leading to the denial of employment or insurance for yourself (or a relative). It also is possible that there could be violations to the security of the computer systems used to store the codes linking the genetic and medical information to you. There also may be other privacy risks that we have not foreseen. While we believe that the risks to you and your family are very low, we are unable to tell you exactly what all of the risks are. A new Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. According to this law, health insurance companies or group health plans cannot request your genetic information or use it to make decisions about your eligibility or premiums; and employers cannot use it in deciding to hire,

promote, or fire you or in setting the terms of your employment. Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. The following link contains details about this law http://www.genome.gov/Pages/PolicyEthics/GeneticDiscrimination/GINAInfoDoc.pdf. You may ask your research team for additional information or a copy of the information from the web site. We believe that the benefits of learning more about myositis outweigh these potential risks; there is a great potential for researchers and health professionals to learn a great deal about the causes of these diseases and from that, to develop better ways to prevent, detect, treat, and cure these illnesses. We will make every attempt to protect your confidentiality and to make sure that your personal identity does not become known.

WHAT TO DO IF YOU DECIDE TO WITHDRAW FROM THIS STUDY

You may withdraw from this study at any time by providing notification to your primary NIH doctor. You may ask to no longer be contacted by us and to not return to the NIH. In this case, we will no longer contact you by phone or mail you any further questionnaires. If you withdraw, upon your written request, we will delete all information obtained about you from our research files and destroy your stored samples. If you decide to withdraw from this study, it will not in any way affect your eligibility for medical care or participation in future research at the NIH.

Once data on your whole genome DNA testing are generated from the samples you have provided, and those data are placed in the Internet-accessible database as described elsewhere in this consent, you may be able to withdraw the data and destroy the samples under certain conditions. If you would like to withdraw from this project, you can contact Dr. Rider at NIEHS and she will destroy any of your remaining tissue samples that have been obtained for the study. In addition, it may be possible for Dr. Rider to remove your DNA testing data and medical information from the Internet database. However, the samples and data that have already been distributed to approved researchers will not be able to be withdrawn.

COMPENSATION

You will be monetarily compensated $100 for the time and inconvenience involved in participation, upon your initial enrollment into the study. For each visit that you return to the NIH to repeat some of the research tests, you will again be monetarily compensated by payment of $100 for each visit. If you enroll through your local health care provider, you and your local health care provider would each receive $100 for the time and inconvenience involved in participation. Compensation would not be made if you are enrolling primarily in another NIH protocol.

CONFLICT OF INTEREST STATEMENT

The National Institutes of Health reviews NIH employees at least yearly for conflicts of interest. The following link contains details on this process http:ethics.od.nih.gov/forms/Protocol-Review –Guide.pdf You may ask your research team for additional information or a copy of the Protocol Review Guide.

This protocol has investigator(s) who are not NIH employees. They are expected to comply with their Institution's conflict of interest policies.

CONSENT TO STORE YOUR SAMPLES FROZEN FOR POSSIBLE FUTURE AND GENOMIC RESEARCH

Thank you for agreeing to participate in this study. Now we would like your permission for the NIH and its research partners to store the remainder of your blood, urine,other samples, and data for possible future research. The frozen samples and data will be stored under a number code. The remainder of the coded specimens may be used for additional studies of myositis and their causes. Only the NIH study researchers will be able to match this code with your name or any identifying information about you. It is possible that your samples or study records may be shared anonymously with other investigators for other research use beyond the scope of this study, including studies of other disorders unrelated to myositis. Such usage will be strictly anonymous, in that no identifying information about you, including your name, will be provided to the researcher, and there will be no way for the researchers to link these samples back to you. Your consent to frozen storage of your samples does not affect your ability to participate in this study.

□ I AGREE to frozen storage for possible future research □ I DO NOT agree to this

Signature of Adult Patient/Legal Representative Date Signature of Witness Date

Sign□ ture of Investigator Date Signature of Witness Date

We would also like your permission to use your child's DNA samples for testing in whole genome association studies that are trying to determine the genetic risk and protective factors for myositis and which also may also determine genetic factors involved in certain complications of the illness or responses to treatment. As part of these studies, you also agree to have your coded genetic information and coded medical information placed in databases accessible by the Internet, as described in the section "*What Will Happen to the Samples or Information that are Collected from this Study*" section on pages 8 - 10 of this document. We will make every attempt to protect your confidentiality and to make sure that your personal identity does not become known. Your consent to participate in the whole genome genetic testing does not affect your ability to participate in this study.

□ I AGREE to whole genome testing of my DNA samples □ I DO NOT agree to this

Signature of Adult Patient/Legal Representative Date Signature of Witness Date

Signature of Investigator Date Signature of Witness Date

OTHER PERTINENT INFORMATION

1. Confidentiality. When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. Policy Regarding Research-Related Injuries. The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. Payments. The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

4. Problems or Questions. If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Principal Investigator, Lisa G. Rider, M.D.; CRC Room 4-2352, Telephone: (301) 451-6272. Other researchers you may call are: Frederick Miller, M.D. PhD, (301) 451-6273 or Anna Engstrom, RN, GNP-BC, (301) 451-6030.

You may also call the Clinical Center Patient Representative at 301-496-2626.

5. Consent Document. Please keep a copy of this document in case you want to read it again.

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/Legal Representative _____ Date _____

Print Name _____

B. Parent's Permission for Minor Patient.

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.
(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/Guardian _____ Date _____

Print Name _____

C. Child's Verbal Assent (If Applicable)

The information in the above consent was described to my child and my child agrees to participate in the study.

Signature of Parent(s)/Guardian _____ Date _____ Print Name _____

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM SEPTEMBER 28, 2010 THROUGH SEPTEMBER 27, 2011.

Signature of Investigator _____ Date _____

Print Name _____

Signature of Witness _____ Date _____

Print Name _____